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Acute kidney injury in cardiac surgery

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ABSTRACT

Introduction. Acute kidney injury (AKI) associated with cardiac surgery is a common postoperative complication that increases the morbidity and mortality substantially. However, there is limited information of AKI after cardiac surgery in our institution. **Material and methods.** We conducted a prospective, observational, and longitudinal analysis of adult patients that underwent to cardiac surgery requiring cardiopulmonary bypass and aortic cross clamp. Patients with preoperative chronic renal insufficiency that were on dialysis, with AKI detected up to 24 h before the procedure, or that received contrast agents 72 h before surgery were excluded. AKI was defined by the AKIN classification. Patients were followed up to 7 days after surgery or before if discharged from the intensive care unit. We analyzed age, sex, body mass index (BMI), co-morbilities, previous cardiac surgery, left ventricular ejection fraction, New York Heart Association class, type of procedure, cardiopulmonary bypass time, cross clamp time and bleeding. **Results.** Our analysis included 164 patients submitted to cardiac surgery. In the follow up, 84% did not have AKI, 11% had AKIN 1 and 2 accompanied by increase in serum creatinine and 6% had AKIN 3. Patients with AKI were older, had a higher preoperative creatinine, plasma glucose level, and a lower left ventricular ejection fraction. All together patients with AKIN had a longer hospital stay and a higher mortality ($p < 0.001$). The preoperative use of insulin was associated with the development of AKI, and there was a higher number of patients with a New York Heart Association class III and IV for heart failure in the more sever forms of AKI ($p = 0.01$). The logistic regression analysis revealed that patients with a high preoperative blood urea nitrogen (> 20 mg/dL) creatinine level (> 1 mg/dL), uric acid (> 7 mg/dL) and lower albumin (< 4 g/dL) or lower intraoperative hemoglobin (< 8 g/dL) had a higher risk for postoperative AKI. **Conclusions.** The prevalence of AKI in our Institute is of 17%. Patients with AKIN 2 and 3 had a higher mortality and a longer stay in the intensive care unit. The major risk factors for AKI development were identified.

Insuficiencia renal aguda en cirugía cardiaca

RESUMEN

Introducción. *La lesión renal aguda (LRA) es una complicación postoperatoria común de la cirugía cardiaca y se asocia con mayor morbilidad y mortalidad. No se conoce en nuestra institución la incidencia y factores perioperatorios asociados al desarrollo de LRA en pacientes sometidos a cirugía cardiaca.* ***Material y métodos.*** *Estudio prospectivo, longitudinal, observacional, realizado en pacientes de ambos sexos, > 18 años, sometidos a cirugía cardiotorácica con circulación extracorpórea (CEC) y pinzamiento aórtico. Se excluyeron pacientes con diagnóstico de insuficiencia renal crónica en diálisis prequirúrgica, LRA 24 h previas a la cirugía y medio de contraste en las 72 h previas a la cirugía. Se eliminaron los pacientes que fallecieron en las primeras 24 h poscirugía. De los registros clínicos se obtuvieron la edad, sexo, índice de masa corporal (IMC), comorbilidades, fracción de expulsión del ventrículo izquierdo (FEVI), clasificación de la NYHA y diversas variables transoperatorias. Para determinar LRA se utilizó la clasificación de AKIN.* ***Resultados.*** *Se incluyeron 164 pacientes. El 17% presentó LRA. Los pacientes con diagnóstico de LRA tuvieron mayor edad promedio, mayor creatinina y glucosa basal y una menor FEVI, así como mayor tiempo de estancia posquirúrgica y mortalidad ($p < 0.001$). Como factores preoperatorios, el uso de insulina se asoció de manera significativa con la categoría de LRA. Se observó mayor frecuencia de pacientes clasificados en estadio III y IV de insuficiencia cardiaca por NYHA en las categorías de mayor severidad de LRA ($p = 0.01$). Mediante análisis de regresión logística simple se encontró asociación estadísticamente significativa entre BUN (preoperatorio) > 20 mg/dL y la probabilidad de tener LRA. Asimismo, otras variables que mostraron asociaciones significativas fueron Cr > 1 mg/dL, ácido úrico > 7 mg/dL, albúmina sérica < 4 g/dL y hemoglobina mínima transoperatoria < 8 mg/dL.* ***Conclusiones.*** *Los pacientes con LRA estadio 2 y 3 tuvieron mayor mortalidad y estancia en terapia intensiva. Las condiciones prequirúrgicas que sí se asociaron con* *el desarrollo de LRA fueron: edad, creatinina basal mayor, niveles de albúmina y ácido úrico y la FEVI.*

Key words. Acute renal failure. Tubular necrosis. Creatinine. Dialysis.

Palabras clave. *Insuficiencia renal aguda. Necrosis tubular. Creatinina. Diálisis.*

INTRODUCTION

Despite the exponential growth of cardiovascular hemodynamics as a therapeutic tool for various heart diseases, cardiac surgery with an extracorporeal circulation pump remains the most frequently performed surgical procedure worldwide.[1] Like all surgical procedures, cardiac surgery is not without potential complications. One such complication is the development of acute kidney injury (AKI) due to ischemia, of particular importance in extracorporeal circulation, which can occur in the range of 1 to 30% of patients.[2-6] The causes of AKI are multifactorial, but ischemia/reperfusion during extracorporeal circulation plays a key role.

Both the percentage of patients who develop AKI in various centers and the severity of this complication vary, ranging from a seemingly harmless mild and transient elevation of serum creatinine to a complete loss of function requiring renal replacement therapy by dialysis. According to various series, between 2 and 10% of patients undergoing cardiac surgery will eventually require postoperative dialysis,[2-7] which increases the mortality rate up to 50-80%.[8] In fact, the development of severe AKI is a dreaded complication because despite advances in cardiopulmonary bypass techniques and critical patient management, morbidity and mortality associated with AKI have not changed significantly in the past 25 years.[3,6,8] In addition to metabolic and hemodynamic consequences, AKI also prolongs hospital stay, increases the risk of infections and has a significant effect on the cost of care.[10]

Postoperative AKI presents more serious implications than what had been previously believed for many years, as it was thought that postoperative elevations in serum creatinine that did not require dialysis were not important and that even patients who required dialysis for AKI recovered ad integrum. However, numerous studies in recent years have shown that this is not the case. On the one hand, we now know that even a minimum increase in postoperative serum creatinine is associated with increased mortality in the first month after surgery.[11] In addition, AKI is an important risk factor for the development of chronic kidney disease.[12-14] In this regard, epidemiological studies have shown that patients who develop elevated postoperative creatinine levels demonstrate a significantly increased probability of developing end-stage renal disease in the future, even though they might not need renal replacement therapy (dialysis); this risk is also higher in patients who require dialysis.[15] Because of these reasons, it is necessary to evaluate the status of AKI in our environment in order to implement programs that might lead to a lower incidence of this complication.

Several studies have assessed the prevalence and risk factors associated with the development of AKI. The type of surgery, female gender, congestive heart failure, type II diabetes mellitus, peripheral vascular disease, preoperative use of the intra-aortic counterpulsation balloon pump, chronic obstructive pulmonary disease, emergency surgery and elevated preoperative serum creatinine are the most frequently reported risk factors.[3,9,16]

Our group previously carried out studies in experimental animals, which suggested that mineralocorticoid receptor blockade with spironolactone could be useful to prevent or reduce AKI due to ischemia, even after exposure to renal ischemia.[17-19] Thus, knowing the situation in our environment is necessary in order to implement these potential therapies in the clinic. However, no prospective studies have been designed specifically to determine the prevalence of AKI in patients undergoing cardiac surgery at our institution and to identify perioperative factors associated with its development. Therefore, the purpose of this study was to determine the incidence and risk factors for AKI in a prospective cohort of patients undergoing cardiac surgery.

MATERIAL AND METHODS

This was a prospective, longitudinal, and observational study designed to determine the incidence and risk factors for AKI in patients who underwent cardiovascular surgery due to various causes at the Instituto Nacional de Cardiología Ignacio Chávez. We excluded patients with advanced chronic kidney disease who were placed on dialysis prior to the surgical procedure, patients with AKI criteria within 24 h prior to the surgical procedure, and patients who had been administered iodinated contrast media in the previous 72 h at a dose higher than 5 mL/kg for each mg/dL of SCr. In-hospital reoperation cases were included only for the first surgical event. The elimination criteria consisted of patients who required further surgery within seven days after the surgical procedure, those requiring the use of intravenous contrast solutions, and those who died within the first 24 h after cardiac surgery.

Patients

Adults who underwent elective cardiac surgery from October 10, 2010 to June 31, 2011 were included in this study. Informed consent was deemed unnecessary because this was an observational study that involved no risk and no cost to the patient.

Measurements

The following data were collected on baseline on the day before surgery: anthropometric measurements, vital signs, history of comorbidities, current drugs and the serum levels of hemoglobin (Hb), hematocrit (Hct), leukocytes, platelets, fasting glucose, creatinine, uric acid, albumin, sodium and potassium. The left ventricular ejection fraction (LVEF) measurement from the last echocardiographic analysis report was recorded. The surgical period was conducted at the discretion of the surgical and anesthesiology team. Data recorded in the immediate postoperative period, including the procedure performed, duration of extracorporeal circulation (pump), aortic clamping time, surgical complications and other findings, were entered into the database.

After surgery and according to the intensive care unit (ICU) postoperative routine, urinary volumes were recorded on an hourly basis, verifying uresis in mL/kg/hr on each shift (3 times daily). In addition, serum creatinine and blood urea nitrogen (BUN) levels were recorded every 24 h, as these values are routinely determined for patients remaining in the ICU.

Definition of variables

The development of AKI was defined according to universally accepted criteria shown in table 1.[20] The types of cardiac surgery that were recorded included valve replacement, coronary artery bypass graft (CABG) surgery, combined surgery (valve replacement surgery and CABG), and other surgeries (closure of atrial or ventricular communications, tumor resection, etc.). Patients were followed-up during the first 7 days after cardiac surgery.

Statistical analysis

The cohort was initially classified into the following 4 subgroups:

- No AKI.
- AKI stage 1-2, which was defined solely by changes in urinary volume without changes in SCr (these patients presented decreased urinary volumes that were successfully managed with volume replacement, without subsequent changes in serum creatinine).
- AKI stage 1-2 due to changes in SCr; and
- AKI stage 3.

Significant differences were found between continuous variables in these patients using an analysis of variance with the nonparametric Kruskal-Wallis test. The comparison of categorical variables for the 4 subgroups was performed using the chi-square test. In an additional analysis, the group without AKI (n = 84) was compared to patients from subgroups 3 and 4, who developed AKI according to elevated serum creatinine levels (n = 28). The Fisher's exact test (2-tailed) was used to test for differences in categorical variables between the two groups (no AKI *vs.* AKI). An unconditional logistic regression analysis was performed to estimate the probability of AKI in accordance with pre-and intraoperative variables. A p value < 0.05 was considered statistically significant. The SPSS/PC V17.0 statistical program (Chicago, IL) was employed for analysis.

RESULTS

As shown in figure 1, 206 patients who consecutively underwent cardiac surgery were included dur-ing the study period. A total of 42 patients were excluded for the following reasons: perioperative death in the first 24 h (5 patients), lack of a baseline urine sample (7), incomplete baseline data (2), because it was decided not to perform aortic clamping and therefore no cardiopulmonary bypass during the surgical procedure (13), and due to the cancellation of surgery for various reasons (15). The final study sample consisted of 164 patients.

In this cohort, 51% of the patients undergoing cardiac surgery were assigned to group 1, i.e., those who did not develop AKI, while 32% were assigned to group 2, i.e., those who developed AKI stage 1 to 2 defined only by transient decrease in urine volume. In addition, 11.5% of the patients developed

AKI stage 1-2 due to elevated SCr (group 3), and only 6% developed AKI stage 3 (group 4) (Figure 1).

Table 2 shows the general features of the study population, classified by their type of kidney injury. The mean age of the patients was 52.9 ± 16.6 years, with the patients who developed AKI stage 3 presenting a significantly older age. Body mass index and the presence of diabetes mellitus did not demonstrate a significant difference in the AKI group, although there was a trend for a higher prevalence of diabetes in the population that developed AKI. Similarly, preoperative serum glucose levels were higher in the AKI stage 3 group, but this difference did not reach statistical significance. Baseline SCr levels were lower in patients who did not develop AKI (0.89 ± 0.22 mg/dL) than those with AKI, and this level was significantly increased in patients who developed AKI stage 3 (1.31 ± 0.41 mg/dL) ($p < 0.001$). Other preoperative variables that showed statistically significant differences between AKI groups included BUN ($p < 0.0001$) and serum potassium ($p = 0.01$). There was a trend for serum albumin ($p = 0.07$). There was no difference in sex distribution between groups, and there were also no differences in the history of diabetes mellitus, systemic arterial hypertension, systemic vascular disease, acute myocardial infarction, peripheral vascular disease, neoplasia and immunosuppressive therapy. The use of insulin as part of prior treatment was significantly associated with AKI ($p = 0.01$). In addition, greater numbers of patients were classified as having heart failure (NYHA stage III and IV) in the most severe AKI categories ($p = 0.01$).

As shown in table 3, we observed no statistically significant difference in the percentage of patients who had previously used medications such as diuretics,

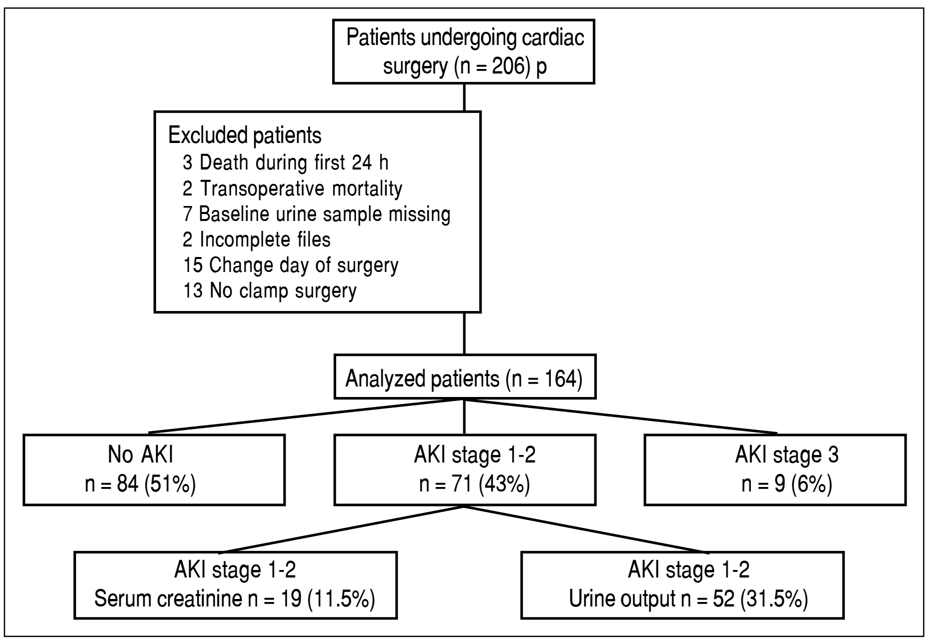

Figure 1. *Studied cohort for acute kidney injury after cardiac surgery.*

Table 1. Classification and staging systems for AKI.[20]

Stage	Serum creatinine criteria (SCr)	Urine output criteria
1	Serum creatinine increase ≥ 0.3 mg/dL or increase to 1.5-2.0-fold from baseline	< 0.5 mL/kg/h for 6 h
2	Serum creatinine increase > 2.0-3.0-fold from baseline	< 0.5 mL/kg/h for 12 h
3	Serum creatinine increase > 3.0-fold from baseline OR serum creatinine ≥ 4.0 mg/dL with an acute increase of at least 0.5 mg/dL or need for RRT	< 0.3 mL/kg/h for 24 h or anuria for 12 h. Or need for RRT

AKI: acute kidney injury. AKIN: AKI Network. RRT: renal replacement therapy.

Table 2. Patient baseline characteristics.

Characteristics	Total Px (n = 164)	No AKI (n = 84)	AKI 1-2 urine output (n = 52)	AKI 1-2 creatinine (n = 19)	AKI 3 (n = 9)	p
Age (years)	52.9 ± 16.6	50 ± 16.8	55.25 ± 15.5	53. 1 ± 17.5	66.9 ± 11.7	0.02
Male, n (%)	82 (50)	39 (46.4)	28 (53.8)	11 (57.9)	4 (45.4)	0.72
Female, n (%)	82 (50)	45 (53.6)	24 (46.2)	8 (42.1)	5 (55.6)	0.72
BMI (kg/m^2)	25.9 ± 4.3	25.3 ± 4.14	26.6 ± 4.13	26.6 ± 5.94	25.7 ± 4.04	0.61
Diabetes mellitus, n (%)	31 (18.7)	15 (17.6)	7 (13.5)	6 (31.6)	3 (33.3)	0.23
Insulin-requiring diabetes, n (%)	6 (3.7)	1 (1.2)	2 (3.8)	1 (5.3)	2 (22.2)	0.015
Hypertension	65 (39.3)	29 (34.1)	20 (38.5)	10 (52.6)	6 (66.7)	0.16
NYHA, n (%)*						0.002
Class I-II	134 (83)	75 (92)	42 (82)	11 (58)	6 (67)	
Class III-IV	27 (17)	7 (8)	9 (18)	8 (42)	3 (33)	
Baseline creatinine (mg/dL)	0.94 ± 0.27	0.89 ± 0.22	0.95 ± 0.26	0.94 ± 0.26	1.31 ± 0.41	0.001
Baseline LVEF (%)	56.9 ± 12.53	57.4 ± 12.5	58.4 ± 11.9	52.7 ± 14.2	50.57 ± 11.4	0.23
Preop glucose (mg/dL)	102.7 ± 30.5	103.3 ± 27.6	99.8 ± 25.75	94.1 ± 25.8	135.03 ± 67.2	0.017
BUN (mg/dL)	19.47 ± 9.41	18.24 ± 8.35	18.91 ± 9.47	20.25 ± 8.37	31.98 ± 12.13	0.002
Uric acid (mg/dL)	6.27 ± 2.17	5.84 ± 1.93	6.55 ± 2.42	6.63 ± 1.98	7.97 ± 2.22	0.10
Albumin (mg/dL)	4.27 ± 0.47	4.3 ± 0.35	4.17 ± 0.52	4.19 ± 0.47	3.7 ± 0.65	0.07
Total bilirrubin (mg/dL)	0.85 ± 0.51	0.87 ± 0.62	0.85 ± 0.37	0.79 ± 0.32	0.71 ± 0.27	0.69
K^+ (mEq/L)	4.32 ± 0.41	4.34 ± 0.35	4.31 ± 0.46	4.13 ± 0.47	4.71 ± 0.37	0.01
Hb (g/dL)	13.7 ± 1.9	14.0 ± 1.9	13.7 ± 2.1	13.4 ± 1.7	13.0 ± 1.0	0.21
Hto (%)	41 ± 5.7	42 ± 5.0	40 ± 6.2	40 ± 4.4	38 ± 4.3	0.11

* Three patients were not classified according NYHA.

NSAIDs, ACEI/ARA2, spironolactone, and statins between the groups with and without AKI. In the immediate postoperative period, NSAIDs were administered to three patients without AKI, as well as one from the AKIN 1-2 group but none from the AKIN 3 group.

The following transoperatory variables were assessed: extracorporeal circulation (pump) time, aortic clamping time, bleeding, and low hemoglobin as a hemodilution factor. None of these variables showed statistically significant differences between groups (Table 4). However, we observed an increase in the postoperative length of stay at the ICU for AKI stage 1-2 patients with increased SCr levels (group 3) and AKI stage 3 patients (group 4) ($p < 0.001$). A total of ten patients died, with an overall mortality rate of 6%. However, it should be noted that no patient in group 1 or group 2 died during the postoperative period, whereas 6 out of 19 patients in group 3 and 4 out of 9 patients in group 4 died during the first postoperative days, yielding mortality rates of 31 and 44%, respectively. This finding reveals the significant mortality associated with the development of AKI ($p < 0.001$).

Table 5 shows the results obtained after reclassifying the cohort into only two groups: those without AKI (originally group 1) and those with AKI due to elevated serum creatinine (originally groups 3 and 4). In patients with diabetes mellitus, the analysis showed a difference that was not statistically significant between groups, with prevalence values of 32% in the AKI group *vs.* 18% in the control group ($p = 0.12$). However, the use of insulin and the presence of systemic arterial hypertension showed significant differences between the groups ($p < 0.05$). There was also a higher prevalence of heart failure (NYHA stage III and IV) in the AKI group ($p = 0.001$), and one-third of the patients in the AKI group had a history of previous cardiac surgery, compared to 11% in the non-AKI group ($p = 0.03$) (Table 5). There was no difference in the type of surgery between AKI groups.

Table 6 shows the results of logistic regression analysis for the preoperative and intraoperative

Table 3. Preoperative medication.

Medication	Total Px n = 164 (%)	No AKI n = 84 (%)	AKI 1-2 Urine output n = 52 (%)	AKI 1-2 Creatinine n = 19 (%)	AKI 3 n = 9 (%)	p
Diuretics	81 (49)	37 (43.5)	28 (53.8)	11 (58)	5 (55.6)	0.45
NSAID	13 (7.8)	8 (9.4)	3 (5.8)	1 (5.3)	1 (11.1)	0.51
ACEI/ARBs	99 (60)	53 (62.3)	28 (53.8)	13 (68.4)	5 (55.6)	0.88
Spironolactone	35 (21)	17 (20)	9 (17)	7 (36.8)	2 (22.2)	0.73
Statins	52 (31.5)	26 (30.5)	19 (36.5)	3 (15.8)	4 (44.4)	0.63

Table 4. Transoperative variables.

Variables	Total Px (n = 164)	No AKI (n = 84)	AKI 1-2 Urine output (n = 52)	AKI 1-2 Creatinine (n = 19)	AKI 3 (n = 9)	p
Pump time (min)	109.7 ± 46.3	108 ± 41.8	107.7 ± 45.6	125.8 ± 60.2	104.7 ± 62.8	0.48
Clamp time (min)	77.3 ± 36.6	78.6 ± 34.2	77.07 ± 39.9	75.33 ± 37.7	69.7 ± 42.6	0.91
Bleeding (mL)	929.9 ± 622	937.5 ± 653	898 ± 591	961 ± 528	972 ± 765	0.97
Minimal Hb (mg/dL)	9.23 ± 5.51	8.89 ± 2.04	10.6 ± 1.42	7.84 ± 1.89	8.02 ± 1.24	0.21
Post-operative						
ICU stay (days)	4.6 (1-41)	3.4 (1-22)	3.2 (2-8)	8.89 (1-41)	15.7 (4-33)	<0.001
Hospital mortality n (%)	10 (6.0)	0	0	6 (31.5)	4 (44.4)	<0.001

Table 5. Comparison between No AKI and AKI Serum creatinine (included subgroups 3 and 4).

Variable	No AKI, n = 84 n (%)	AKI 1-2 SCr + AKI 3, n = 28 n (%)	p
Male	39 (46.4)	15 (53.6)	0.522
Female	45 (53.6)	13 (46.4)	
Diabetes mellitus	15 (17.9)	9 (32.1)	0.119
Insulin-requiring diabetes	1 (1.2)	3 (10.7)	0.048
Hypertension	29 (34.5)	16 (57.1)	0.045
Congestive heart failure	1 (1.2)	1 (3.6)	0.439
Heart failure class NYHA, n (%)			
I	26 (31.7)	4 (14.3)	0.001
II	49 (59.8)	13 (46.4)	
III	6 (7.3)	9 (32.1)	
IV	1 (1.2)	2 (7.1)	
Previous cardiac surgery	9 (10.7)	8 (28.6)	0.033
Previous myocardial infarction, n (%)			
1-4 weeks	6 (7.1)	2 (7.4)	0.98
> 4 weeks	10 (11.9)	3 (10.7)	

values according to reference values. A statistically significant association was found between preoperative BUN > 20 mg/dL and the probability of developing AKI (OR = 4.34, 95% CI 1.75-10.75, p = 0.002). Likewise, other variables that showed significant associations included preoperative SCr > 1 mg/dL (OR = 2.65, 95% CI 1.10-6.41, p = 0.04), preoperative uric acid > 7 mg/dL (OR 4.09, 95% CI 1.26-13.33, p = 0.02), serum albumin < 4 g/dL (OR 3.85 95% CI 1.10-13.47, p = 0.06), and minimum intraoperative

Table 6. Univariable associations with AKI.

Variable	No AKI, n = 84 n (%)	AKI1-2 SCr + AKI 3, n = 28 n (%)	OR	C I 95%		p
Preoperative						
Hb < 12 mg/dL	16 (19)	5 (18.5)	0.966	0.317	2.94	1.000
Hto < 36	14 (17)	6 (22)	1.429	0.488	4.179	0.568
BUN > 20 mg/dL	21 (26.3)	17 (61)	4.342	1.752	10.75	0.002
Serum Cr > 1 mg/dL	23 (27.4)	14 (50)	2.65	1.097	6.410	0.037
Uric acid > 7 mg/dL	11 (19.6)	8 (50)	4.091	1.256	13.328	0.024
Serum albumin < 4 mg/dL	9 (14.8)	6 (40)	3.852	1.101	13.473	0.063
LVEF < 60%	51 (68)	18 (75)	1.412	0.497	4.009	0.615
Transoperative						
Min Hb < 8 g/dL	22 (31)	15 (57.7)	3.037	1.203	7.671	0.020

hemoglobin < 8 g/dL (OR 3.04 95% CI 1.20-7.67, p = 0.02).

In the multivariate model using the method of progressive steps for the variables of diabetes, hypertension, age, insulin use, heart failure and temperature, only two variables were selected: heart failure (adjusted OR 2.35, 95% CI 1.17-4.76; p = 0.017) and temperature (adjusted OR 6.62, 95% CI 1.02-42.50, p = 0.047). The remaining variables did not reach statistical significance.

DISCUSSION

AKI associated with cardiac surgery represents a serious postoperative complication that significantly increases the risk of death or subsequent development of chronic kidney disease.[1-15,21] According to the literature, the incidence of AKI in patients undergoing cardiac surgery ranges between 1 and 30%.[2-6,8,9] In the present study, the incidence of AKI was 48.7% (80 of 164) when considering all AKI patients (groups 2, 3 and 4). However, this figure was likely overstated, as the 52 patients who were initially classified with AKI stage 1-2 according to a transient decrease in urine volume did not demonstrate any consequences on renal function. If we only consider patients classified as AKI stage 1-2 with elevated serum creatinine levels and those classified as AKI stage 3, this incidence was 17% (28 of 164), which is more consistent with what has been reported in the literature.[1,3-6,9] The percentage of patients requiring renal replacement therapy (RRT) was 6% (AKI stage 3), which is also similar to that reported in the literature.[2,3-9] One limitation of this study was that we only included patients who underwent elective surgery, and it is likely that the AKI incidence would be higher in a cohort that included patients undergoing emergency surgery, in which renal perfusion pressure is likely not optimal.

Similar to what has been observed in other studies,[9,11,15] patient mortality and length of stay in the surgical intensive care unit were higher in the group that developed AKI. Our data showed that mortality, which was calculated at 6%, occurred only in patients with AKI. In other words, all patients in this cohort who died had developed postoperative AKI. In our cohort of patients requiring RRT, 70% underwent valve replacement and 30% underwent bypass surgery. However, we found no gender differences upon comparing the total number of surgeries and the number of patients who developed AKI, although previous reports[9,16] have shown that 65.4% of AKI cases correspond to female patients when no distinction of the type of cardiac surgery is made. Our subgroup analysis further showed that gender distribution in our cohort was similar. In addition, 90% of the patients who died underwent valve replacement surgery; of these cases, 50% received aortic valve replacement, 20% received mitral and tricuspid valve replacement, 10% received mitral valve replacement and 10% received aortic valve replacement surgery combined with Coronary Artery Bypass Graft. In total, bypass surgery presented a mortality rate of 10%.

The level of baseline or preoperative serum creatinine has been shown to be an independent risk factor for the development of AKI in the postoperative period.[1-9,22] Our observations agree with this finding, as a significant difference was found regarding the preoperative creatinine level (p < 0.001) in the 3 AKI groups. Regarding the other preoperative variables, we observed that the probability of developing

AKI was associated with levels of BUN > 20 mg/dL, uric acid > 7 mg/dL and serum albumin < 4 g/dL. These data suggest that in our patients undergoing cardiac surgery, those demonstrating evidence of reduced preoperative renal function and an elevated state of inflammation were more likely to develop AKI in the postoperative period.

Regarding the relationship between the use of certain medications and the subsequent development of AKI in the postoperative period, there is some evidence to suggest that certain drugs that alter renal blood flow can lead to tubular injury and, through interactions with additional factors, increase the risk of AKI.[17,23-24] However, we found no relationship between the previous use of medications, such as diuretics, NSAIDs, angiotensin converting enzyme blockers, angiotensin AT1 receptor blocker, spironolactone or statins, and postoperative development of AKI. In fact, insulin was the only drug used in the preoperative period that was related to the development of AKI, and this result is similar to those reported in other series.[3,7] The association between insulin administration and the increased risk of postoperative AKI can likely be explained by the fact that the use of insulin is related to the severity of diabetes, which is associated with an increased risk of postoperative complications.[1,9-10,24]

Metha, *et al.*,[1] assessed the association between AKI and the use of an aortic counterpulsation balloon pump and observed an 11.8% incidence of AKI in this patient group. In another series,[9] 23% of patients with AKI had received treatment with an aortic counterpulsation balloon pump compared to 7% who did not develop AKI. In our series, only 2.4% of all patients required a counterpulsation balloon pump, and only 0.6% of these cases were associated with AKI. However, the number of patients in this subgroup was low because our cohort was composed of patients who underwent elective surgery; therefore, most of our patients were in stable condition.

Coronary Artery Bypass Graft surgery is performed more frequently in patients with decreased LVEF compared to other patients undergoing cardiac surgery.[2,3,5,6] In our cohort, the mean LVEF in patients undergoing bypass surgery was 52%, in comparison to 58% in patients undergoing other types of surgery. In addition, patients in AKI group 3 (LVEF 52.7% ± 14.2) and AKI group 4 (LVEF 50.6% ± 11.4) demonstrated lower LVEF values as compared to patients in group 1 (LVEF 57.4% ± 12.2) and group 2 (LVEF 58.4% ± 12), although this difference was not significant difference ($p = 0.20$). However, there was a higher prevalence of heart failure (NYHA stage III and IV) in AKI groups 3 and 4 ($p = 0.001$).

Variables associated with the surgical period, such as aortic clamping time, extracorporeal circulation time, and a minimum hemoglobin level of 8 mg/dL, have been shown in several reports to be directly related to the development of AKI.[1,9,25,26] In our cohort, there was no significant difference between groups regarding these variables; however, in the logistic regression analysis, minimum intraoperative hemoglobin < 8 g/dL was identified as a risk factor for the development of AKI (OR 3.04 95% CI 1.20-7.67, $p = 0.02$). One possible mechanism by which low hemoglobin concentrations are associated with AKI could be the reduced diffusion of O_2.[23-26]

CONCLUSIONS

The incidence of AKI and renal replacement therapy in adult patients during the postoperative period after receiving cardiac surgery with extracorporeal circulation at our institute was 17 and 6%, respectively, similar to what has been reported in the literature. In addition, AKI was significantly associated with mortality. In patients who developed AKI, we observed significantly higher levels of preoperative serum creatinine, BUN and uric acid; lower values for serum albumin; an advanced NYHA stage classification; lower LVEF; and reduced perioperative hemoglobin values < 8 g/dL.

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